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ABSTRACT

PULMONARY HYPERTENSION AND ARTERIOSCLEROSIS.

Abstr. Rudolph Koucky

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Introduction

Increased tension within the pulmonary vessels is a common condition in the terminal stages of almost every cardiac decompensation. Such a state is usually of short duration and the increased tension is not sufficiently important to deserve consideration as an individual condition. There are occasions, however, in which the pulmonary hypertension becomes a formidable factor, and part of the clinical picture is produced by this condition. Not infrequently the longstanding hypertension produces marked changes in the lung and heart which are independent of the primary disease. Finally, a small group of cases occur in which the changes in the pulmonary vessels appear to be primary and the clinical picture is not correctly diagnosed either by the roentgenologist or the clinician unless this pathological entity is kept in mind.

In the case presented today, the pulmonary arteriosclerosis was not diagnosed during life because of an accompanying asthma which overshadowed the findings and symptoms. The presence of this asthma and the long period of treatment with adrenalin may prove to be interesting possibilities in the evolution of our case.

History

Almost immediately after systemic (generalized) arteriosclerosis was first described, it was observed that pulmonary vessels were not involved. The peculiarity aroused comment and speculation and this interest has continued to present day. The subject therefore is an old one, however, today

less is known about pulmonary hypertension and arteriosclerosis than is known about the systemic type. Ljungdahl gives a complete review of the history of this condition. Buisson (1803), Ondral (1829), Otto (1830), Lobstein (1835) were the earlier writers and the list includes most of the subsequent prominent pathologists. Dittrich's work (1850) still authoritative. In recent years, additional stimulus was given to the subject by the South American writers following Ayerza's teachings. Apparently, these men tried to introduce a new disease. However, it seems to be only a revival of old ideas with a new interpretation.

Pathology

Pulmonary hypertension and arteriosclerosis show the same changes in the vessels as are seen in the systemic type. In the large vessels, there are the same atheromatous plaques under the intima. These are circumscribed or diffuse. These plaques may become calcified. Dilatation of the vessel accompanies these changes. In the smaller vessels, there occurs a diffuse thickening under the intima which obstructs the lumen in proportion to the severity of the change. Thrombosis sometimes occurs at the site of a plaque or in the terminal parts of a vessel beyond a point of complete closure. Microscopically, the process is primarily limited to the intima. There is an overgrowth of loose, fibrous tissue, the interspace of which is filled with fat containing cells. This is spoken of as a fatty metamorphosis of the intima.

The elastic tissue and muscle are only secondarily involved, if at all. The spirochetes cannot be demonstrated (even by Warthin). This absence of change in the media of the vessel and the absence of spirochetes is interpreted as ruling out syphilitic processes such as had been advanced by the South American authors. Hyalinization of this subintimal fibrous tissue takes place in the small vessels. The lumen frequently is reduced to small slit.

The secondary changes produced by the sclerosis of the vessels are widespread. The lung parenchyma, as would be expected, shows little change. (All of the pulmonary arteries to a lung may be ligated at once without producing gangrene. The bronchial arteries off the aorta provide sufficient blood supply.) Sclerosis of the bronchial arteries is not described as part of the picture and therefore fibrosis of the lung parenchyma does not occur.

The heart suffers the most severe changes. The obstruction necessarily is accompanied by difficulty in forcing the blood through the lung. A marked hypertrophy of the right ventricle takes place. The left ventricle is not affected. Since the sclerosis is a slow process, hypertrophy compensates for the disturbance for a long time. Eventually, and usually suddenly, the compensation is broken and dilation of the ventricle and auricle take place (see our case). Congestion of the viscera, ascites and edema follows. Pressure in the azygos veins is increased. In the same manner, the coronary veins are engorged and hydropericardium results. This latter finding at autopsy appears to be very frequent.

Etiology

The following table is a classification based on etiology.

I. Primary
II. Secondary
  mitral disease,
  congenital heart disease
  emphysema (senile, inflammatory types)
  chronic pulmonary infection with fibrosis
  spine deformities
  pleuro-pulmonary fibrosis.

The "primary" pulmonary arteriosclerosis is as its name indicates unassociated with any other disease. The lung, heart and viscera show only changes secondary to the arteriosclerosis. This process appears to be a primary disease. No known etiological factor has been proven. One line of thought has been developed which is given a good deal of emphasis. As Moschcowitz states, arterio-

sclerosis is preceded by an increased tension within the vessel (exclusive of senile changes and lipoid deposits such as occur in children). According to this theory, some process must be present in the pulmonary vessels causing an increase of tension which eventually leads to the sclerosis. On this basis, congenital hypoplasia of pulmonary veins has been advanced and discarded since there is no evidence of back pressure in the lung capillaries. Repeated spastic contractions of the muscles of the arteries is another theory. (See MacCallum or Ljungdahl). This suggests the spastic theory of pathogenesis ascribed to asthma. (Note in our patient the associated asthma!) An antigen of bacterial protein or foreign protein produces a "local" sensitivity. Reapplication of the antigen may produce spasm of the arterioles. The spasm produced by adrenalin may be so severe as to produce necrosis of the intima (Ljungdahl). (Significance of adrenalin in our case?) Subsequent arteritis may be superimposed on the changes started by the spasm. Experimentally, plaques have been produced by superimposing an infection on changes induced by adrenalin.

Arteritis (arteritis deformans, etc.) of pulmonary vessels also has been presented as a cause. This is difficult to prove or disprove. Such arteritis has not been found in most cases.

Syphilis, according to the South American writers, was considered to be the cause. Proven cases of syphilis show a much different lesion in pulmonary vessels (in media and adventitia). Warthin could find no evidence of syphilis in the cases he studied. The idea of syphilitic origin has been discarded. It is retained in the theory that syphilis is a sensitizing antigen producing spasm of the arteriolar muscles.

The pulmonary valves have been normal in all cases and this therefore is not a causative factor.

Congenital hypoplasia and other congenital changes are also theories.

In India, primary pulmonary arteriosclerosis seems to be more frequent than in other countries. Several cases in young individuals have been described. Syphilis is said to be common and Rogers states that this is usually cited as the etiological basis but probably without adequate proof. In 1909, he described 10 cases, 9 of which were below 40 years of age.

Summary of Etiology

Although no single factor has been proven, spasm of the arteries either with or without infection appears to be the most acceptable cause of the arteriosclerosis.

Secondary Types

The etiological factors in this group are quite clear. Hypertension which is followed by changes in the intima is accepted as the cause. The hypertension is mechanical in these cases. Mitral disease (especially stenosis) is the most frequent cause. The abnormal flow of blood mechanically produces increased tension in the pulmonary vessels. In addition, the pulmonary fibrosis produced by congestion decreases the capillary bed within the lung. In congenital heart disease (open intraventricular septum or open ductus arteriosis), the full force of the aortic pressure is transmitted to the pulmonary arteries. The normal pulmonary pressure is said to be one-sixth of the aortic. Senile emphysema and emphysemas due to inflammatory changes belong in the same category as chronic lung fibrosis. In all such cases, the fibrosis of the parenchyma reduced enormously the capillary bed resulting in a mechanical obstruction. Uncomplicated asthma does not produce fibrosis and does not belong in this class. This disease does not produce pulmonary arteriosclerosis in the uncomplicated forms. (In our case, we must regard the arteriosclerosis as the primary type. No parenchymal fibrosis is present.)

Pleural fibrosis has been frequently reported as a cause. Most such cases have an associated fibrosis of lung which produces the constriction of the vessels. In all these cases,

the principle is the same: mechanically produced hypertension in the pulmonary circuit followed by secondary sclerosis of the vessels. (See Ljungdahl or Moschcowitz).

Other systemic diseases produce pulmonary arteriosclerosis only in so far as they reproduce the conditions described above. Nephritis may produce hypertension, cardiac failure and the n pulmonary hypertension. Diabetes is sometimes associated because of the frequent coronary involvement and subsequent heart failure.

Senility is accompanied by arteriosclerosis of the larger pulmonary vessels, without much change in the small ones. There is never the severity seen in the aorta and it usually produces no symptoms. In 52 cases of severe systemic sclerosis, the pulmonary vessels were involved in 30. Some change was observed almost always after the age of 70. The age at onset of senile sclerosis is considerably more than of the systemic type.

In Ljungdahl's series, the primary lesion was as follows:

Chronic pulmonary disease	45
Acquired heart disease (mainly mitral stenosis)	35
Chronic nephritis (15 cases)	5
Open ductus arteriosis	1
Diabetes (6 cases)	1

It may be concluded that in any condition in which there is a mechanical obstruction to a free flow of blood through the lungs and heart that some degree of pulmonary hypertension and arteriosclerosis will result.

Clinical and Roentgenographic Diagnosis

Pulmonary arteriosclerosis is not entirely a pathological curiosity. Many clinical men feel that the condition gives rise to definite diagnostic findings whose recognition makes an otherwise confusing syndrome quite clear.

These reports of the clinical features have been collected and tabulated by Ulrich. For the sake of brevity, the table presented here is combined from the tables outlined by this author.

Subjective symptoms

1. History suggests heart disease.
2. Repeated hemoptysis (streaking, etc.) without evidence of infarct.
3. Repeated and tenacious bronchitides.
4. Easily provoked dyspnea.
5. Cyanosis (may be absent early) which is marked and out of proportion to other symptoms and findings.
6. Other pulmonary symptoms only when pulmonary disease is primary cause.

Physical findings

1. Heart enlarged to right.
2. Pulmonary souffle over entire chest.
3. Palpable pulsation in intercostal spaces.
4. Abnormal prolongation of second sound.
5. Reduplication and accentuation of a second sound.
6. Increased dulness to left of upper sternum with pain on pressure (Posselt).
7. Polycythemia, increased hemoglobin.

Radioscopic Evidence

1. "The dome of the diaphragm": A down and up movement of the diaphragm synchronous with systole and superimposed on its own respiratory movements.
2. Increase of hilar shadows.
3. Abnormal bulging of right auricle.
4. Increase in volume of the pulmonary artery.
5. The phenomena of the dome of the hilus.
6. Series of dark trails through the lung fields animated by contractions (dome of artery).

All of these symptoms and findings are easily explained by the pathological findings. The enlarged right heart, cyanosis, polycythemia, etc. are quite obvious results as described above.

The "dome" of various structures (hilus, arteries and diaphragm) observed under the fluoroscope are very unusual. The term "animated", sometimes used, is descriptive of the process. The vessels move much like the toruous sclerotic vessels of the temples of elderly men under the impulse of the heart beat. The sclerotic vessels of the lung move in like manner producing a to and fro short movement of the hilus, the arterial shadows (roentgenoscopic) in the lung fields and of the entire lung. The latter movement is transmitted to the diaphragm. These movements are synchronous with the heart beat.

The pulmonary souffle or bruit is heard over the entire chest but is most clearly heard in the left second interspace, in the right interspace and in the right side. This bruit resembles the noise heard over a placenta, or over a highly vascular and enlarged spleen, thyroid or liver. This sound is thought to arise in the pulsating pulmonary vessels.

The pulsation in the intercostal space is transmitted from the pulsating lung. It is felt best in the thin areas of the chest: upper spaces, anteriorly near the sternum, axillae and low in the posterior chest wall.

The triad of findings - pulsation in the intercostal spaces, pulmonary souffle and the dome of the diaphragm have been added to the literature by Ulrich.

(How often do we overlook these findings in our cases of longstanding mitral disease, emphysema, etc.?)

Prognosis

The onset of arteriosclerosis is definitely changes the prognosis both in mitral disease and in chronic pulmonary conditions. In deformities of the thoracic spine, the presence of this complication and therefore a possible right heart failure must be kept in mind. Investigation may show that some of the deaths, particularly postoperative deaths in chronic lung disease and marked thoracic spine deformity, may be on this basis.

Summary

1. Pulmonary arteries ordinarily are not involved by arteriosclerosis.

2. Senile atheromatous changes do occur but they come on only in advanced age and never in the severe degree seen in the aorta.

3. In certain pathological changes, pulmonary hypertension and arteriosclerosis may occur.

4. Those with a known preceding condition are called "secondary"; those in which the cause is unknown are described as "primary".

5. The best known causes of the condition are mitral disease, pulmonary fibrosis, chronic inflammatory emphysema, deformities of the chest, congenital heart disease and pleural fibrosis.

6. The pathogenesis in these cases is a mechanically produced hypertension which is followed by the degenerative changes in the vessels.

7. In the primary type, attempts have been made to find a similar case for hypertension. The most accepted theory is spasm of the arterioles associated with or followed by an arteritis. These changes can be reproduced experimentally by adrenalin in the presence of an infection.

8. In our case, the presence of bronchial asthma and a long intake of adrenalin may be etiological factors.

9. The pathology is essentially the same in pulmonary arteriosclerosis as in the systemic type. Large vessel changes and arteriolar changes are present in the pulmonary vessels similar to the other type.

10. The right heart suffers the greatest damage. Enormous hypertrophy takes place. Compensation is adequate for long periods. When it fails, dilation of the right heart and congestion of the viscera, ascites, edema, etc. take place.

11. From clinical observations, the vessels of the lung move with each heart beat much like senile sclerotic vessels of the forehead.

12. The clinical picture can be quite definite if all the characteristic features are looked for. The

history and a brief examination suggests heart disease.

13. The "animated" moving pulmonary vessels give rise to a palpable impulse in the intercostal spaces, a pulmonary bruit and an up and down movement of the diaphragm and lung hilus.

14. This triad is peculiar to pulmonary hypertension.

15. The prognosis is definitely worse when pulmonary arteriosclerosis sets in.

II. CASE REPORT

BRONCHIAL ASTHMA. PULMONARY ARTERIOSCLEROSIS. PNEUMOCOCCIC PNEUMONIA.

Path. Koucky

Case is of white male, 35 years old, admitted to Minnesota General Hospital 3-10-33, expired 3-22-33 (12 days).

Infection followed by asthma

1930 - Had upper respiratory infection. During this illness, suddenly developed dyspnea and wheezing. First appearance of asthmatic symptoms. Shortly thereafter moved to Wyoming. No relief from asthmatic attacks. Remained there for 3 years without any change. Asthmatic attacks recurred 2 to 3 times a week, usually lasting 1 to 4 hours. As time went on, some decrease in frequency. On arising, usually some cough with expectoration of whitish sputum.

Prolonged adminis ration of adrenalin

Adrenalin through this period gave considerable relief. Frequent changes of diet without benefit. No seasonal variation observed except that hot sultry weather made symptoms worse.

Asthma, upper respiratory infection

3-10-33 - Admitted. Physical examination: Bony overgrowth over right orbital ridge. Throat - somewhat reddened; enlarged tonsils; posterior nasal discharge. Thyroid-enlarged. Chest - tactile fremitus increased throughout; no areas of dulness; diffuse rales and wheezes heard in both lungs; increased spoken voice sounds. Heart - definite cardiac enlargement to left and right; faint diastolic murmur and definite systolic murmur. Abdomen - no tenderness or masses. Extremities - indurated, scarred skin on upper left arm and forearm; slight edema about knees. Neurological examination - negative. Laboratory: Urine - heavy cloud of albumin, many wbc's. Blood - Hb. 109%, wbc's 12,000, Pmn's 66%, L 29%, M 1%, E 4%. N.P.N. - 43.4 mg. per 100 cc. of blood.

X-ray of chest and sinuses

There is a marked increase in the broncho-vascular markings throughout both lung fields, particularly at the bases, where there is considerable pleurisy, possibly some bronchiectasis. There is a definite enlargement of the heart, left ventricular type. There is a definite thickening of the mucous membrane of both maxillaries and both sets of ethmoids, there is some cloudiness of the sphenoids also, frontals appear fairly clear. Conclusions: Chronic inflammatory process, both bases, with diaphragmatic pleurisy. Possibly some bronchiectasis. Enlarged heart. Bilateral maxillary, ethmoidal and sphenoidal sinusitis.

Unusual heart

6 Ft. Heart - Measurements: transverse thoracic 30, ml 13, mr 5.8, total 18.18, long. 21. The heart is greatly enlarged and of a rather peculiar globular shape. Esophagogram shows only a very slight displacement of the esophagus entirely out of proportion to the size of the heart, indicating that there probably is no particular mitral valve disease. The appearance suggests rather an aortic lesion but the possibility of a combined aortic and mitral lesion must be considered. Findings in lungs previously reported are again shown. Conclusions: Cardiac enlargement, atypical, probably aortic lesion. Practically no displacement of esophagus.

Progress

3-15-33 - Daily asthmatic attacks with wheezing, difficulty in breathing, etc. Relief with adrenalin which is administered 1 or 2 times a day. Persistent albuminuria ranging to 2+1. N.P.N. - 43.4 mg. Dilution-concentration test - specific gravity 1.016 to 1.030. P.S.P. - 45% excretion at end

of 2 hours. Temperature within normal limits.

3-17-33 - Asthmatic attacks much worse. Now requiring more adrenalin daily.

3-18-33 - Asthmatic state present almost throughout entire day. 8 injections of adrenalin given without great deal of relief. Morphine sulphate gr. 1/4 finally given with some improvement.

3-19-33 - Condition better. Normal temperature. Difficulty in breathing still present. 3 injections of adrenalin.

Pneumonia

3-20-33 - Temperature suddenly rises to 103.2. Respirations rise to 40 and pulse to 120. Uncomfortable all day. Difficulty in breathing, expectorating a great deal of white sputum. Adrenalin does not give relief. Given morphine which finally improved the condition. Examination of chest shows a small patch of coarse rales in left base posteriorly. Throat is quite red. X-ray of chest - pulmonary congestion present without evidence of pneumonia. Blood - Wbc's 32,900. First appearance of cyanosis. Scant pulmonary findings.

3-21-33 - Examination of lungs shows no further change. Pain in left lower chest. Tired and weak. Perspiring profusely. Slightly cyanotic. 11 A.M. - Cyanosis definite. Oxygen tent started. Patient unusually drowsy. Temperature 103.6. Examined several times, no evidence of a pneumonic process. Pulse 160. Respirations 20 to 40. Blood - wbc's 62,000, Pmn's 82%, M 8%, L 10%. Clinical impression: Bronchopneumonia.

Rapid exitus. Heart condition still indefinite.

3-22-33 - Definite dulness in left lower chest. Breath sounds not transmitted. Chest full of wheezing ronchi and fine rales. Condition becoming critical. More cyanotic. Difficulty in breathing. Respiratory rate dropped to 20. No response to any treatment. 12:40 P.M. - Expired. Clinical impression: Bronchial asthma. Pansinusitis. Bronchopneumonia, left base. Heart disease of undetermined type.

Autopsy

Scars

Body is well-developed, nourished, white male, 35 years of age, measuring 175 cm. in length and weighing 165 lbs. Rigor absent. Hypostasis just beginning. No edema, cyanosis or jaundice. Pupils equal, each measuring 5 mm. in diameter. Innumerable, fine scars present over both arms with induration of subcutaneous tissue (due to hypodermic injections). Subcutaneous fat abundant.

Peritoneal Cavity smooth and glistening without excess fluid. Appendix free and shows no inflammatory process.

Diaphragms down.

The diaphragm on the right is at the 6th interspace and the left at the 7th rib.

Pleural Cavities: When thoracic cage is opened, lungs retain volume and do not collapse. Do not meet in midline because heart is very much enlarged and separates the lungs. Pleural cavities are free on both sides and contain no excess fluid. Pericardial Sac smooth, glistening and contains no excess fluid.

Right ventricular hypertrophy and dilation.

Heart is very large, dilated and distended with blood. Measures 23 cm. in widest diameter and weighs 675 grams. Right atrio-ventricular orifice readily admits 4 fingers and measures 16 cm. in circumference. Left atrio-ventricular orifice appears to be of normal diameter. Vessels at base measure as follows: pulmonic 11 cm. in circumference, aortic 8 cm. Musculature of right ventricle is markedly hypertrophied and dilated. Thickness of left ventricle appears approximately normal. It is not dilated. Heart is divided along midline of interventricular septum between 2 atria and the 2 halves are weighed independently. Right ventricle and auricle weigh 370 grams, left ventricle and corresponding auricle weighs 250 grams. (The difference in this combined weight of 625 grams and the original heart weight of 675 grams is due to the trimming off of portions of the large vessels.) Mus-

culature of heart shows no infarction, fibrosis or softening. Mural endocardium is smooth and glistening. Valves are well formed, show no thickening, deformity or vegetation.

Pulmonary arteriosclerosis

Root of Aorta smooth. Pulmonary vessels appear dilated. Right measures 3.75 cm. after 1st bifurcation, left 4 cm. Intima is thickened and raised by several yellowish irregularly outlined atheromatous plaques. These can be seen as far as the vessel can be dissected. They are most conspicuous at the bifurcations of the vessel.

Asthma, pneumonia

Right Lung weighs 540 grams, Left 1050. Left Lung: Left lower lobe completely consolidated. Texture, consistence and appearance resembles in all respects that of a pneumococcic (lobar) pneumonia in stage of gray hepatization. Numerous granular plugs seen in alveoli. Surface of lung is friable and a large amount of gray, purulent material can be scraped away.

Left upper lobe and all lobes of Right Lung have approximately same appearance. These areas are very light, fluffy, distended with air which slowly escapes from the opened bronchi. No interstitial emphysema. Both upper lobes at apex of lateral surface contain numerous subpleural cysts ranging in size from a few millimeters up to 1.5 cm. in diameter. Right lower lobe somewhat heavier than remainder and there appears to be some edema in this part. On cross section, small bronchioles are very prominent within the lung parenchyma. Wall appears thickened. Their lumen is larger than that of normal bronchi. Lumina of all bronchioles shows no bronchiectasis. Walls appear thickened and somewhat edematous. There is reddening of the mucosa. Secondary and tertiary branches of bronchi are filled with stringy, gelatinous mucus. In the lung parenchyma, arteries are prominent and at first glance are mistaken for bronchioles.

Acute congestion

Spleen weighs 300 grams, large, soft and very much congested.

Liver weighs 1750 grams. It has been pushed down by the diaphragm so that about 2/3 of the liver appears below the costal margin. Liver markings are exaggerated. Liver appears congested. No old passive congestion.

Gall-bladder has thin wall and contains no stones. Bile ducts patent.

Gastro-intestinal tract shows only early postmortem changes in esophagus and stomach. No malformation, ulceration, inflammation, tumors or diverticulae present.

Pancreas soft and pink. No cysts, tumor or fibrosis.

Adrenals are usual size. No adenomas, hemorrhages or degeneration.

Each of the Kidneys weighs 150 grams. Capsules strip easily. Kidneys are rather dark, bloody and congested. Surface is smooth. Kidneys do not cut with increased resistance. No scarring or pitting. Pelvic fat not increased in amount. Slight reddening and thickening of mucous membrane of both pelves. Ureters and Bladder appear normal. No cystitis.

Prostate small and soft.

No systemic arteriosclerosis

Aorta is of good caliber throughout. Intima is smooth except along intercostal arteries where there are a few atheromatous plaques.

Lymph Nodes of mesentery and mediastinum not appreciably enlarged.

Permission for examination of Head and Neck - not granted.

Diagnoses

1. Bronchial asthma.
2. Pneumococcic (lobar) pneumonia, left lower lobe.
3. Subpleural cysts and emphysema.
4. Hypertrophy and dilation of right heart.
5. Acute passive congestion of spleen, liver and kidneys.
6. Edema of lungs.
7. Pyelitis, acute.
8. Pansinusitis (clinical).

No left ventricular hypertrophy.

Additional note:

B.J.C. examined heart. It is his opinion that the left heart shows no evidence of either hypertrophy or dilation. Hypertrophy of heart is entirely in right ventricle.

Cultures of bronchi, lung parenchyma, of pneumonic area by streak method on blood agar plates: Cultures of bronchi showed a marked predominance of a pneumococcus which proved to be type III. A few scattered colonies of streptococcus and staphylococcus also present. Cultures of left lower lobe showed a pure culture of pneumococcus which when typed found to be type III.

Microscopic

Left lower lobe shows well expanded alveoli packed with polymorphonuclear leucocytes and fibrin. The bronchioles do not contain purulent material as is common in pneumonia. They are filled with a clear mucus. The marked hypersecretion of the mucous glands and epithelium has apparently washed out the purulent material.

In the remainder of the lung, there is the typical picture of asthma: enormous hypersecretion of mucus in the bronchial epithelium and glands, mucus filling of the bronchioles, thick basement membrane, thick bronchial wall with increase of fibrous tissue and muscle and increase in number of leucocytes. These are chiefly lymphocytes and plasma cells. Eosinophiles, however, are difficult to find. The lung parenchyma shows distended alveoli. There is no fibrosis of the parenchyma.

The pulmonary arteries show a marked thickening of the intima. Some small arterioles are almost completely occluded. The bronchial arteries do not appear to be involved.

III. MORTALITY REPORT Jan., Feb., Mar., 1933.

Malignant

A. Examined

Brain, glioma of	f28
Brain, medullo-blastoma of	f13
Brain, glioma of	m 5
Carcinoma, cervix	f70
Carcinoma, colon	m64
Carcinoma, colon	m78
Carcinoma, gall-bladder	f68
Carcinoma, lung	m50
Carcinoma, prostate	m54
Carcinoma, rectum	f44
Carcinoma, rectum	m50
Carcinoma, rectum	m55
Carcinoma, sigmoid	m37
Carcinoma, stomach	m42
Carcinoma, stomach	m41
Carcinoma, stomach	m52
Carcinoma, stomach	m53
Carcinoma, stomach	m56
Carcinoma, stomach	m47
Hodgkin's Disease	m64
Lymphosarcoma, stomach	m70
Neurofibromatosis	m78
Ovary, malignant cystadenoma	f59

B. Not Examined

Brain, malignant tumor of	m15
Carcinoma, bile duct	f65
Carcinoma, larynx	m66
Carcinoma, ovary	f41
Carcinoma, prostate	m66
Carcinoma, stomach	m50
Carcinoma, stomach	m71
Carcinoma, tongue	f72
Endothelioma, chest	m52
Melanoma, malignant	f52

Non-Malignant

A. Examined

Actinomycosis, generalized	m15
Appendicitis, acute	f 4mo.
Appendicitis, acute	m25
Arteriosclerosis?	m54
Arteriosclerosis?	m70
Ascites, chylous	m 5mo.
Asthma, lobar pneumonia	m35
Birth injury	m 8mo.
Cholecystitis, chronic	m66
Cholecystitis, chronic and cholelithiasis	f67
Congenital abnormalities, multiple	f 1mo.
Congenital heart defect	m 6

Coronary thrombosis, bowel obstruction f71

Diabetes f48
Diabetes, gangrene m72
Diabetes, gangrene m78
Diarrhea, infantile f16da.
Dysentery, bacillary m 3
Encephalitis, acute infectious m17
Endocarditis, bacterial m56
Endocarditis, subacute bacterial m46

Fracture, neck of femur f74

Glomerulonephritis, subacute m17

Hernia, ventral, p.o. atelectasis f34
Hypertension m59
Hypertension m62
Hypertension m62
Hypertension, toxic goiter f56

Leukemia, aleukemic f 2
Leukemia, myeloid m71
Liver, cirrhosis of f69

Malnutrition f17da.
Mastoiditis, acute m25da.
Meningocele, pulm. edema m 9
Myelitis, acute f38

Obstruction, intestinal m11
Obstruction, intestinal f52
Obstruction, intestinal f68
Osteomyelitis of femur m42
Otitis Media, mastoiditis m49

Pneumonia, lobar m59
Pneumonia, lobar; pregnancy f41
Pneumonia, lobar; prostatic obstruction m82
Pregnancy; difficult prolonged labor f28
Premature m 1hr.
Premature m 4da.
Premature f 5da.
Premature m 9da.
Premature m 9da.
Premature m12da.
Premature, mastoiditis m24da.
Purpura, lobar pneumonia f12
Pyelonephritis f 1

Rheumatic fever, acute f21

Septicemia, primary strep. f 2
Stillborn m 0
Stillborn m 0
Stillborn f 0
Stillborn f 0
Stillborn f 0
Stillborn f 0

Tobes Dorsalis m50
Tracheitis, acute ulcerative f38
Tuberculosis, miliary m70
Tuberculosis, pulmonary m49

Ulcer, perforated gastric m66

B. Not Examined

Aortic regurgitation, luetic m53

Bacteremia, acute m44
Birth injury f 3

Cholecystitis, chronic f39
Coronary sclerosis m63
Coronary thrombosis f44

Decompensation, cardiac, cause? m73

Fracture, neck of femur f74

Hydrocephalus, spina bifida f21da.
Hypertension m59
Hypertension m64

Leukemia, lymphatic m31

Nephrosis, chronic m 2

Peritonitis, pelvic f28
Pneumonia, broncho m50
Pneumonia, lobar m72
Pneumonia, lung abscess m56
Prostate, benign hypertrophy m78
Pyelonephritis, chronic m39

Stillborn f 0

	Deaths		Autopsies		%	
	1932	1933	1932	1933	1932	1933
Jan.	21	43	15	31	71	72
Feb.	30	40	25	29	83	73
Mar.	30	36	25	29	83	81
	81	119	65	89	80	76

1932 Oct.Nov. Dec.	119 deaths)	
	81 autopsies)	68%
1933 Jan.Feb.Mar.	119 deaths)	
	89 autopsies)	76%

Comment:

Note higher number of deaths, more examinations, smaller percentage 1933 over 1932. Congratulations for increase from 68 to 76% fall to winter. The large number of malignant not examined still looks strange. Ratios - malignant 70-30, non-malignant 77-23.

IV. THE EFFECTS OF EXERCISE

The evolution of a mechanized society, about which so much is heard at the present time, has brought about changes in the physiologic functions of the man of today as well as in his economic relationships. Hard physical work, once the lot of the majority of people, is gradually being relegated into the category of the less usual experiences of daily life. As a consequence the bodily conditions formerly resulting so largely from muscular work as a part of the customary routine of living are now being developed through voluntary exercise and athletics. It has been stated that athletics consist of physical exercise plus more or less of emotional exercise, while work is likely to involve less and less of the emotions.

A modicum of muscular effort--of work --has always been regarded as wholesome to the healthy organism. There is a widespread belief that certain physiologic advantages and desirable bodily changes are attributable to physical exercises and training. How real are they, and what is their nature? An elaborate discussion of these questions has recently been presented by Steinhaus of the Young Men's Christian Association College of Chicago. As he points out, increases in muscle size, strength and endurance are probably among the best recognized chronic effects of muscular exertion. One cannot proceed far in the consideration of the contractile tissues without being brought face to face with the problems of their blood supply; for through this the removal of waste and the replenishment of energy alone can be insured. The interrelationship between the skeletal muscles and the circulatory apparatus seems to have been recognized by the discoverer of the circulation of the blood. In 1628, Harvey wrote: "The more muscular and powerful men are, the firmer their flesh; the stronger, thicker, denser and more fibrous their hearts, the thicker, closer and stronger are the auricles and arteries." Haldane once remarked that the circulation and respiration may be looked on as the servants of the muscles. Today there are added factors that call for recognition: chemical changes in the blood, adjustments of the respiratory functions, involvements of the endocrine organs, and new coordinations in the nervous system. It has been stated that undoubtedly the greatest and most lasting changes induced by training in man and animal, namely, changes in behavior, take place in the nervous system.

If the thesis that exercise increases the capacity of the organism to perform work is accepted, it becomes interesting to consider the "interlocking division of responsibilities" for this general outcome. The physiologist Lindhard recognizes improvements in strength, in endurance and in sureness of perfection of movement, and he attributes them in general to changes in the muscular system, respirocirculatory system and nervous system, respectively.

According to Steinhaus, increase in strength is no doubt primarily associated with the hypertrophy of muscle in which largely the sarcoplasm participates. Too little is known of the way in which chemical energy is transformed into mechanical energy in the muscle to speculate on how the chemical changes observed in muscle contribute to the increase of strength. Endurance, or the postponement of fatigue, is a measure of the organism's ability to balance catabolic with appropriate anabolic processes. Primarily this means a sufficient supply of oxygen and, secondarily, a food

supply. The modern conception of the chemical details involved in muscle mechanics is sufficiently novel to warrant repetition here. Phosphocreatine, a recently recognized muscle component, is broken down and then resynthesized at the expense of a glycolytic process. Steinhaus postulated the following possible causes of fatigue: (1) Depletion of the phosphocreatine store, as by loss of one or both of its breakdown products. (2) Failure of the resynthesis process as the result of some limitation being set on the production of lactic acid, which most commonly is probably due to the accumulation of lactic acid and therefore to (3) inability to oxidize lactic acid promptly because of a shortage of oxygen. The lactic acid thus accumulated enters the circulation and causes (4) disturbances in carbon dioxide carrying power of the blood, in the respiratory center and in vasomotor regulation, which an increased circulation can only temporarily compensate. (5) Failure of the circulatory and respiratory system to meet these demands.

The various adaptations that facilitate the performance of more exercise and result from a period of "training" bring about increased return of venous blood by active muscles to the heart. This organ is filled more completely, an outcome which, in accord with the "law of the heart," induces stronger systoles. Oft repeated, as Steinhaus points out, this leads to cardiac hypertrophy with corresponding greater stroke volume, resting minute volume, and slower pulse rate. The faster circulation of the blood results in fragmentation of older corpuscles, both red and white, and a consequent stimulation of the corpuscle-producing tissues. The blood corpuscles are thus "trimmed" for greater service. A greater resting minute volume, augmented by the return flow as soon as exercise begins, carries much greater supplies of oxygen to the active tissues, thus providing for the disposition of lactic acid at its source and preventing its entering the circulation in quantities large enough to disturb the equilibrium elsewhere. To bring about the many cardiac, vasomotor and respiratory adjustments a great burden is placed on the nervous system, particularly the autonomic portions. Undoubtedly during exercise these adjustments are mainly due to sympathetic activity. A well ordered program of athletics should aim to elicit gradually these many beneficial reactions without forcing them to the point of detrimental overstrain.

Editorial: J.A.M.A. 100:578-579, (Feb. 25) '32.

According to Williams (Hygiene and Sanitation), W. B. Saunders Co., most sedentary workers "need a program of physical activity consisting of exercise in natural movements supplemented with as much wholesome outdoor exercise as is necessary to provide that margin of motor activity essential to individual health." Natural exercises do not represent a complete system of body building nor do they meet the play requirements of children nor the recreative needs of adults. Natural exercises should be performed on arising in the morning and should be followed by the morning bath.

1. Standing: The feet are parallel to each other, 6 to 8 inches apart, with one foot 3 or 4 inches in front of the other. Stand with the weight on the outer margin. Push the trunk upward and lift the abdominal wall upward. Keep the shoulders relaxed but secure a sensation of extension and lengthening of the body without tensing the muscles.

2. Stretching: A natural movement that straightens the spine, lifts the chest and overcomes the sagging of the abdominal muscles. Push the arms easily upward and rise on the toes as far as possible. Reach up as if trying to get an object from a high place. Next, let the arms sink and the heels touch the floor but retain as long as possible the sensation of extension.

3. Throwing: A natural movement (throwing a ball) chiefly for the purpose of developing coordination and a powerful trunk exercise. Stand with the feet about 2 feet apart with the left about 6 inches in front of the right. Clasp hands lightly, waist high,

shift weight to the right foot, bend the right knee, draw both hands to the right, twist the trunk to the right and turn the head to the right. The left leg is straight and relaxed, and the left heel is off the floor. The trunk is inclined forward. Next, throw with the right hand, twisting the trunk sharply to the left. The force of the throw should turn the body so that the left foot is turned in the direction of the throw. In performing the movement let the muscles simply carry out your desires.

4. Lifting: (Low and high). For low lifting, bend the right knee and reach the arms to the right of the right foot about 12 inches. Next transfer the weight to the left foot and lift the object. For high lifting, reach to the floor with the back flat, lift the object to the left and place it high above the head.

5. Climbing: This movement is a powerful exercise for the legs and secures strong contraction of the abdominal muscles. First reach upward with the arms, raise the right knee forward, and push the body upward on the ball of the left foot. Secure vigorous stretching upward. Next, return to the standing position.

6. Walking: A natural movement performed with movement of the opposite arm and leg. First raise the right knee forward and swing the right arm forward. Next, reverse the position.

7. Running: This is a natural exercise performed on the balls of the feet with vigorous thrusting upward of the knees and free and vigorous swinging of the arms. First, swing the right arm forward and thrust the left knee upward and forward at the same time, pushing the body upward on the ball of the right foot. Next, reverse the position.

8. Jumping: To clear an obstacle or grasp an object above the head, one resorts to jumping. Bend the knee and hip joints and incline the body forward. Swing the arms downward and backward elevating the heels slightly. Next, swing the arms forward and upward and swing into the air.

Comment: With the growing interest in keeping fit and learning how to live, such prescriptions will become commonplace in the near future. It is recommended that the patient should first learn how to do the exercise correctly, next try it only a few times and then repeat it frequently.

V. MEETING

Date: April 20, 1933

Place: Interne's Lounge, 6th Floor, West Building

Time: 12:15 to 1:15

Program: Acute Yellow Atrophy of Liver

Present: 88

Discussion: C. J. Watson
F. Vanzant
B. A. Watson

Theme:

C.J.W.: I think that you have emphasized one of the most important things, the necessity of telling whether the jaundice is intrahepatic or extrahepatic. Unfortunately, galactose tolerance test is not of great help as it is also positive in extrahepatic cases. As long as the obstruction is not complete the quantity of urobilin in the urine is of great help. The output is often enormously over that of extrahepatic obstruction. I am hoping now to be able to give bilirubin by mouth in order to get an artificial source of urobilin and test function in these cases. One of the most important things so far as prophylaxis is concerned is treatment of acute catarrhal jaundice. There is definite relationship between acute catarrhal jaundice and acute yellow atrophy. Remember one case, girl, 18 years of age, had acute mild catarrhal jaundice cleared up nicely, but continued to run large amount of urobilin in the urine for a period of 6 weeks, then out of the clear sky became deeply jaundiced and died after 10 days of acute yellow atrophy. The use of carbohydrates intravenously every day, keeping patient quiet until all signs of liver injury

disappears, is indicated. Urobilin in the urine is of prime importance in prognosis.

F.V.: In our experience at the Mayo Clinic, and reading over literature, one point stood out. In the history of cincophan poisoning there was failure to take food in the 24 hours preceding development of jaundice. Not all cincophan cases fatal. One man had jaundice for 6 months, fluctuating jaundice, and then recovered. Is not a question of overdosage but of sensitization?

B.A.W.: I was in Montreal when 6 out of our 9 cases came in. You can't say it is safe to give cincophan and give it a long time. First brought to attention by doctor's wife who came in vomiting with pyelitis?, seen by clinician who diagnosed lobar pneumonia. Jaundice, bile stained casts in the urine, bilirubin, direct van den Bergh, all present. Asked how uterus emptyed but because of lobar pneumonia refused to do it. Woman died. Lobar pneumonia turned out to be a huge liver. Next case coming in was a woman off the streets, pregnant about the same time with bile stained casts in the urine. Immediate emptying of uterus and intravenous glucose--recovered. Atophan developed in Canada. After these two cases came in we had 4 cases of acute yellow atrophy due to drugs, all coming from same town. It seemed rather unusual. Checking up revealed that a druggist was doing a wholesale business with atophan. All patients gave history of taking drug from a period of 2 months to 3 years. At McGill they stopped using drug. Bile stained casts in the urine and a lower urea in the presence of direct van den Bergh, particularly if patient is pregnant, is diagnostic of acute yellow atrophy of liver.

Gertrude Gunn,
Record Librarian.